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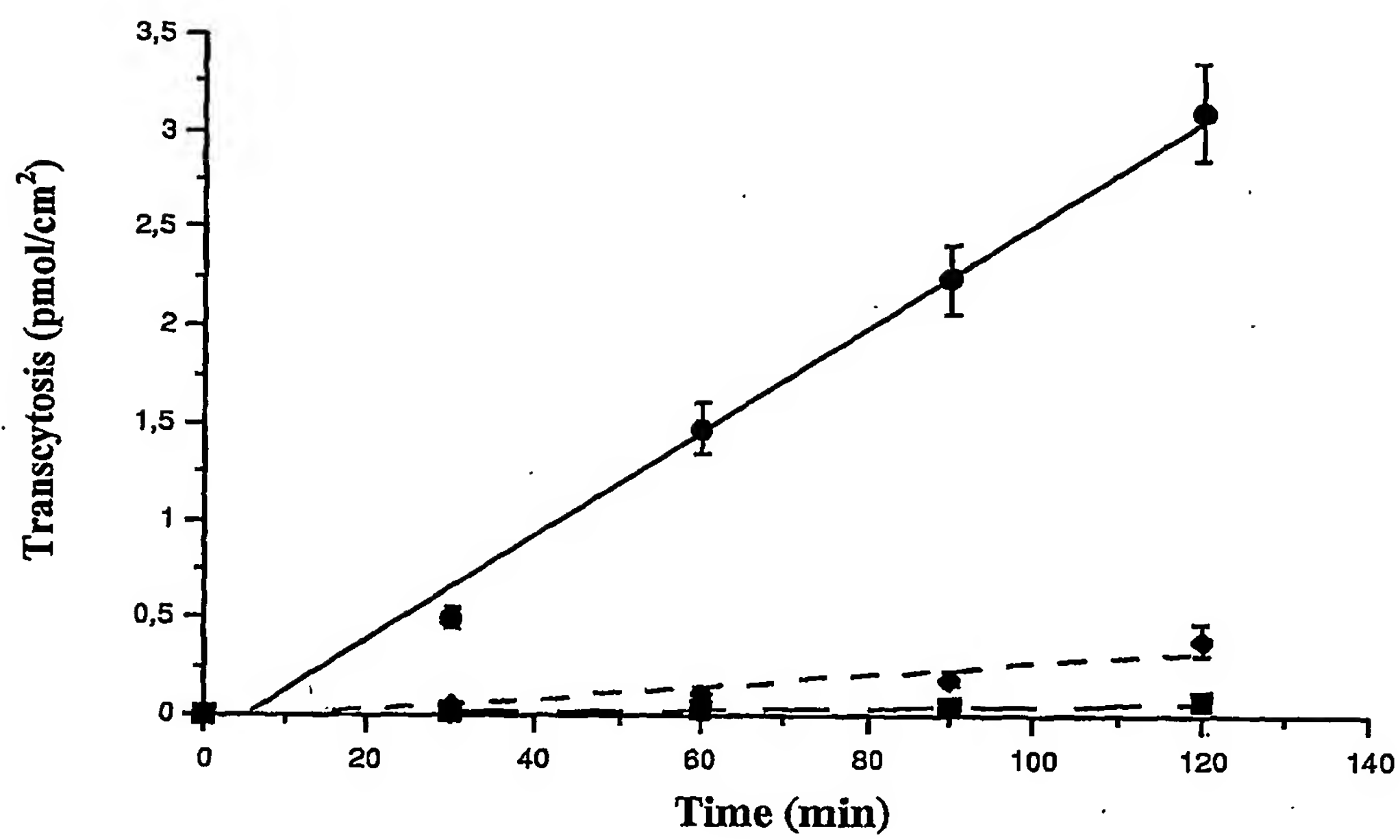


FIG. 1

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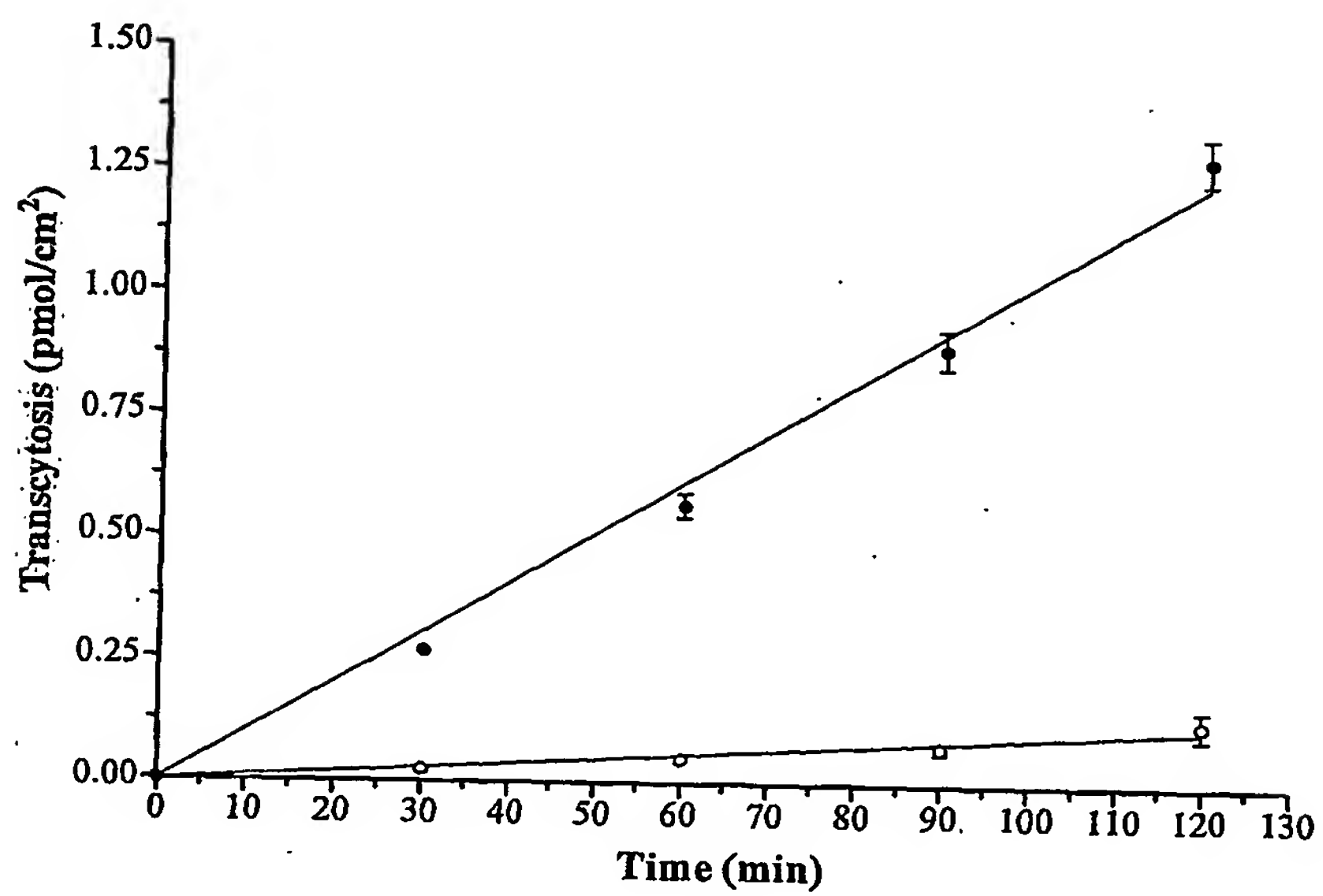


FIG. 2

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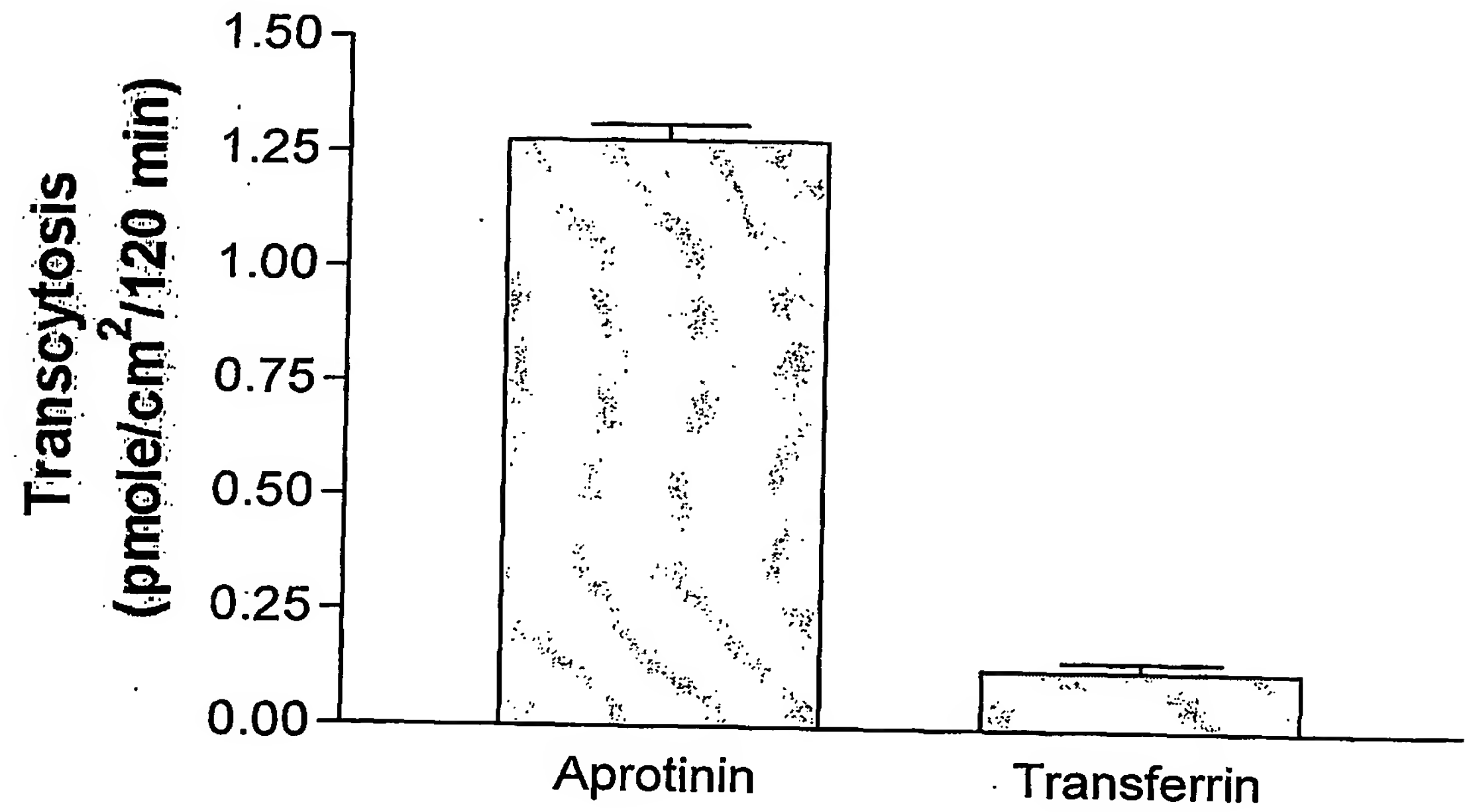


FIG. 3

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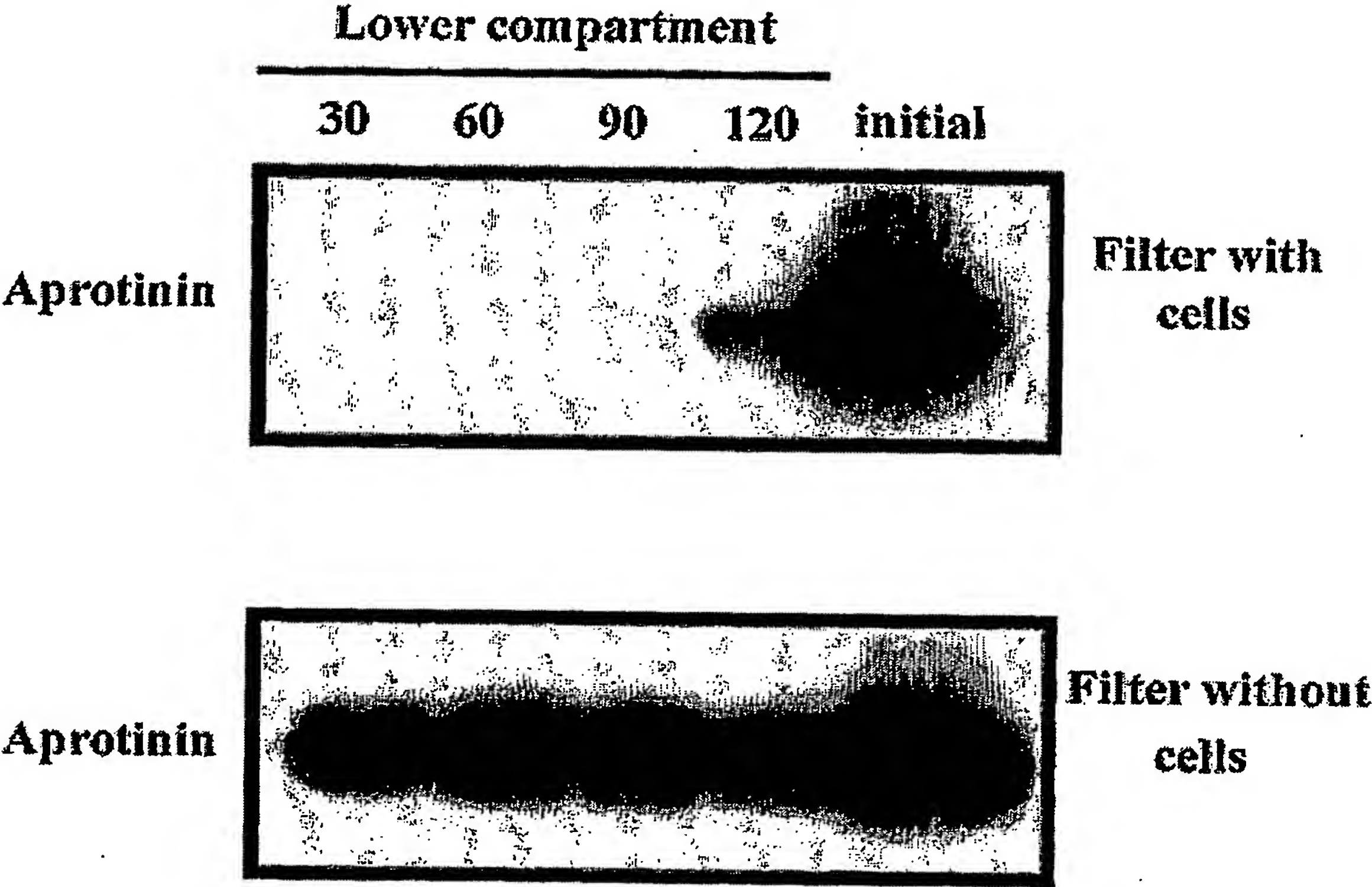


FIG. 4

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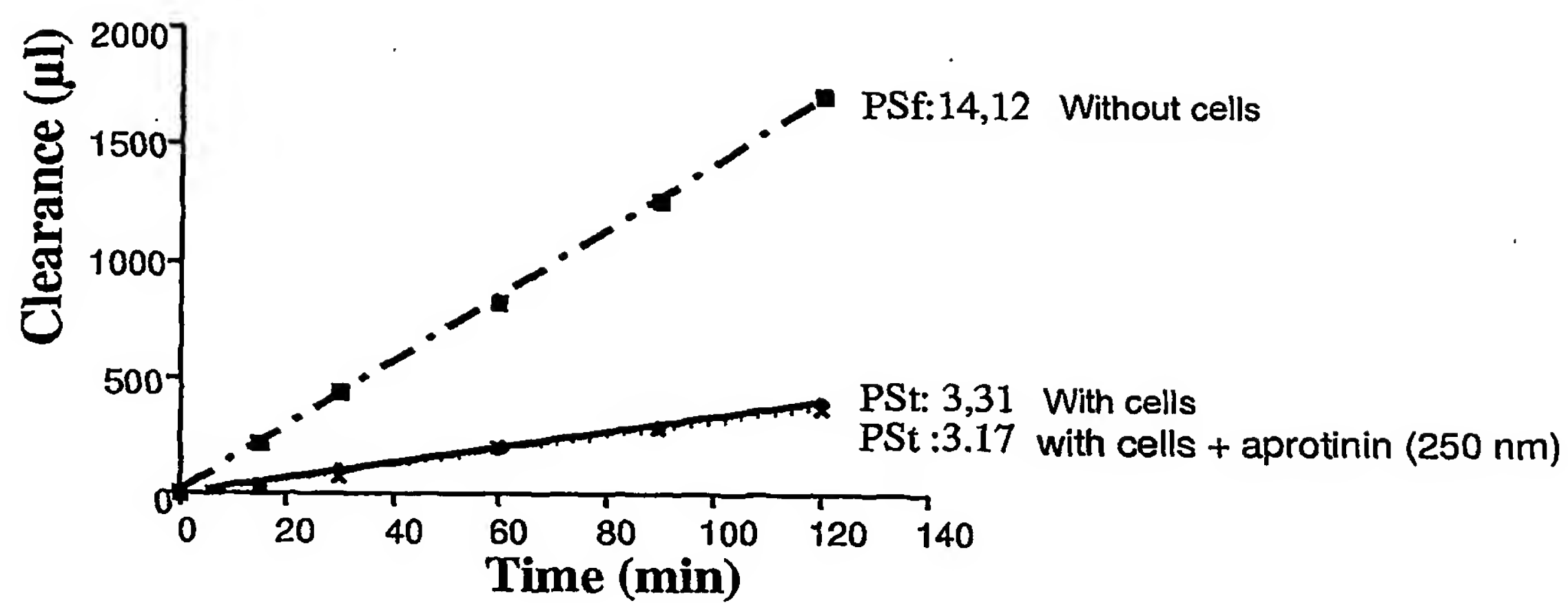


FIG. 5

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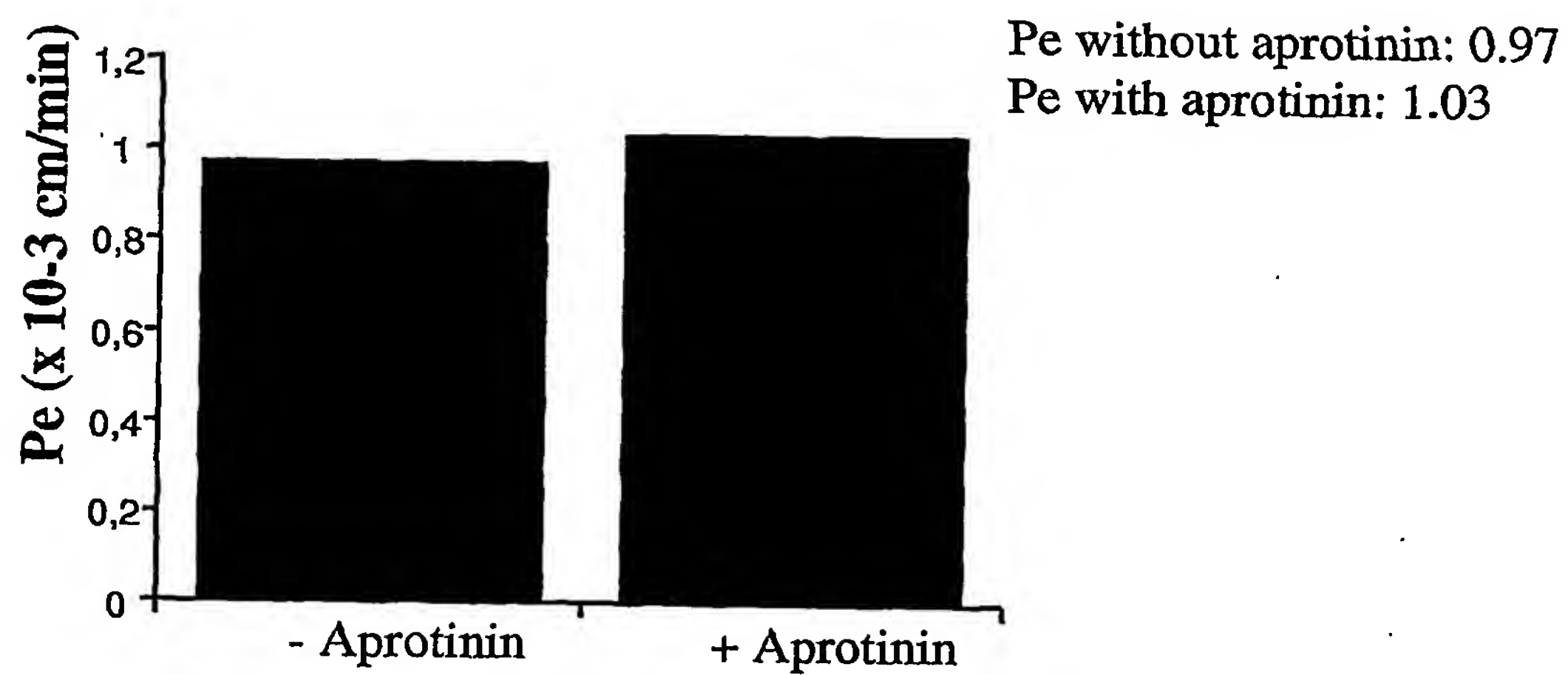


FIG. 6

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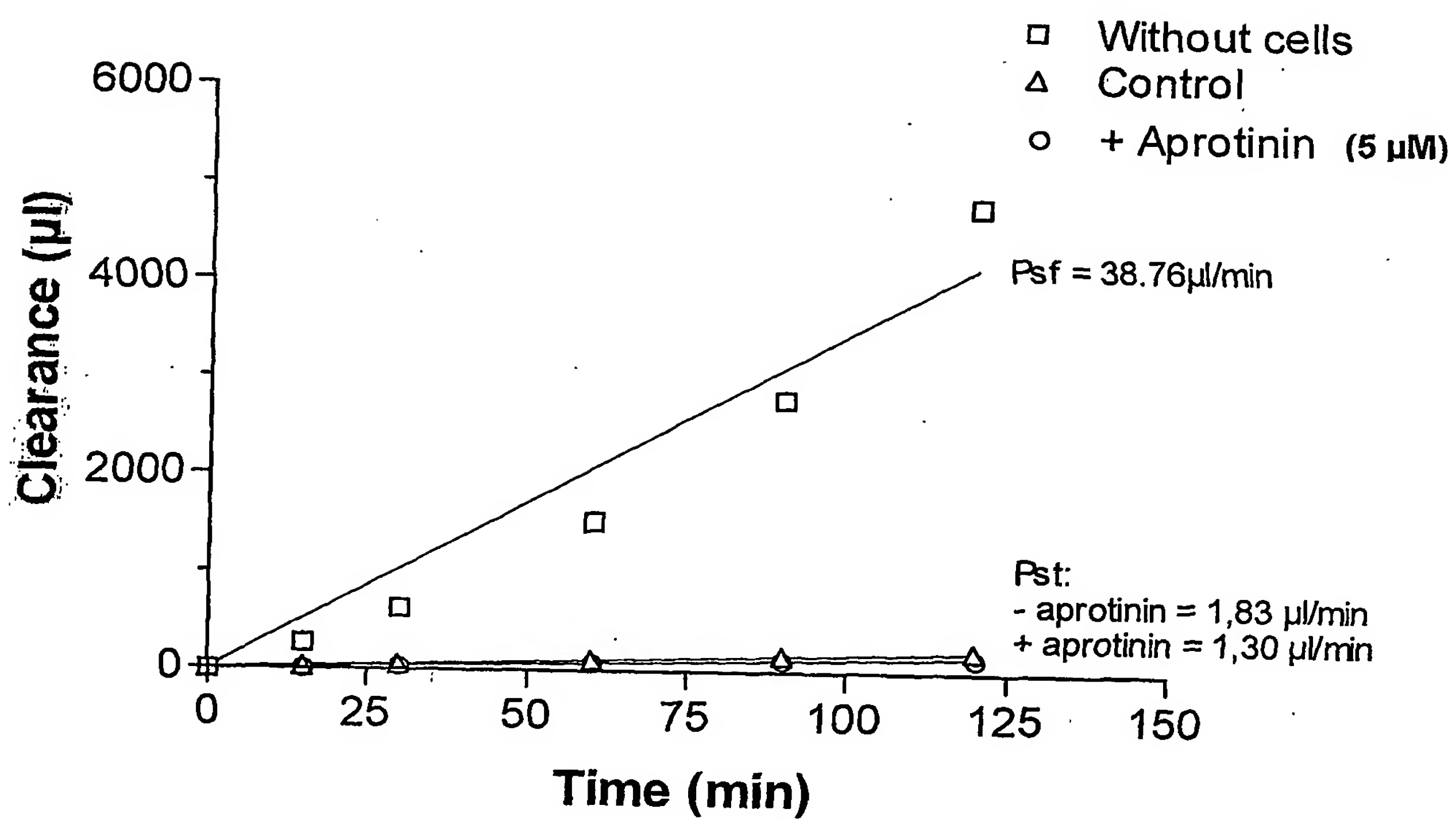


FIG. 7

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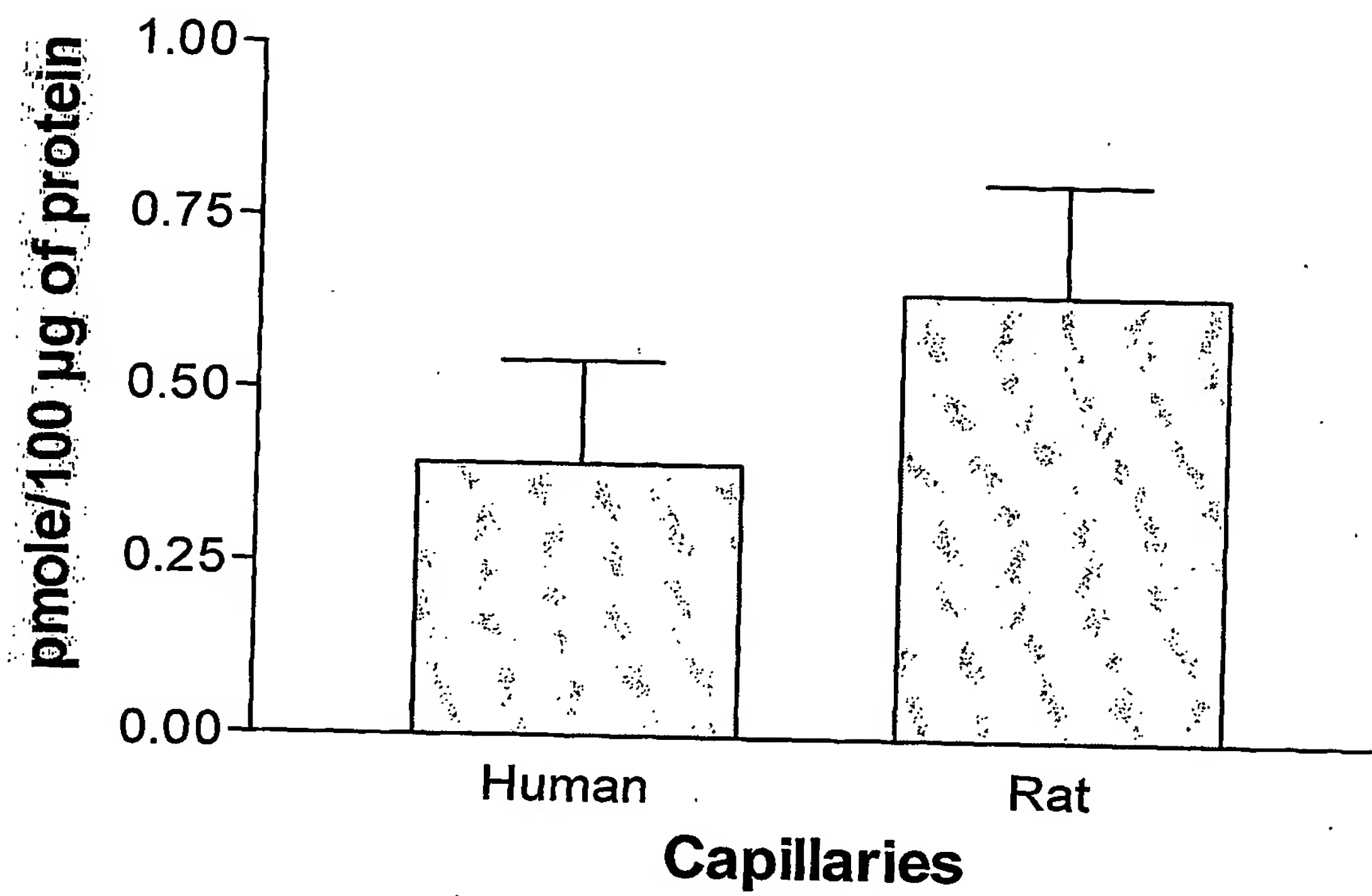


FIG. 8

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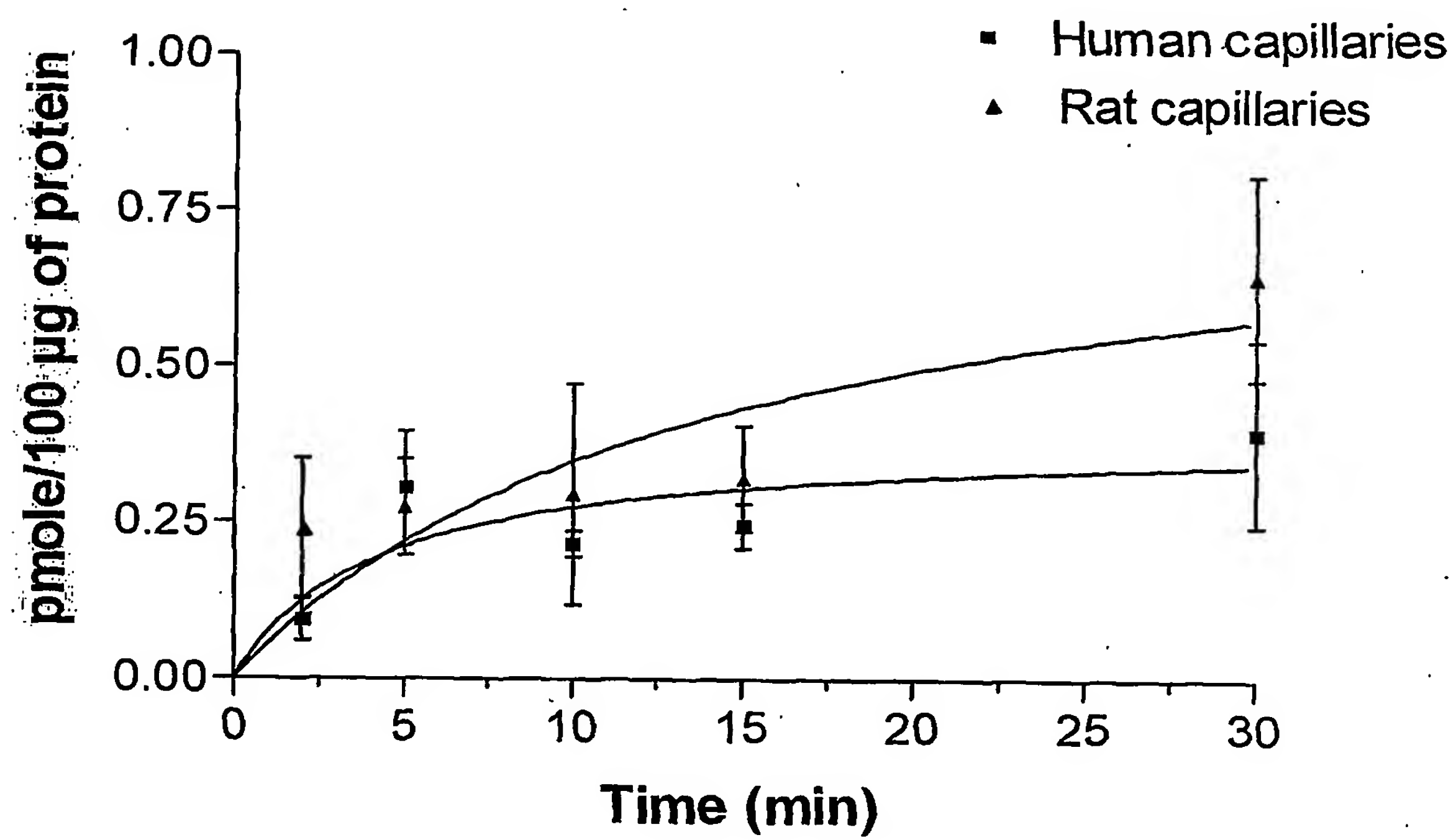


FIG. 9

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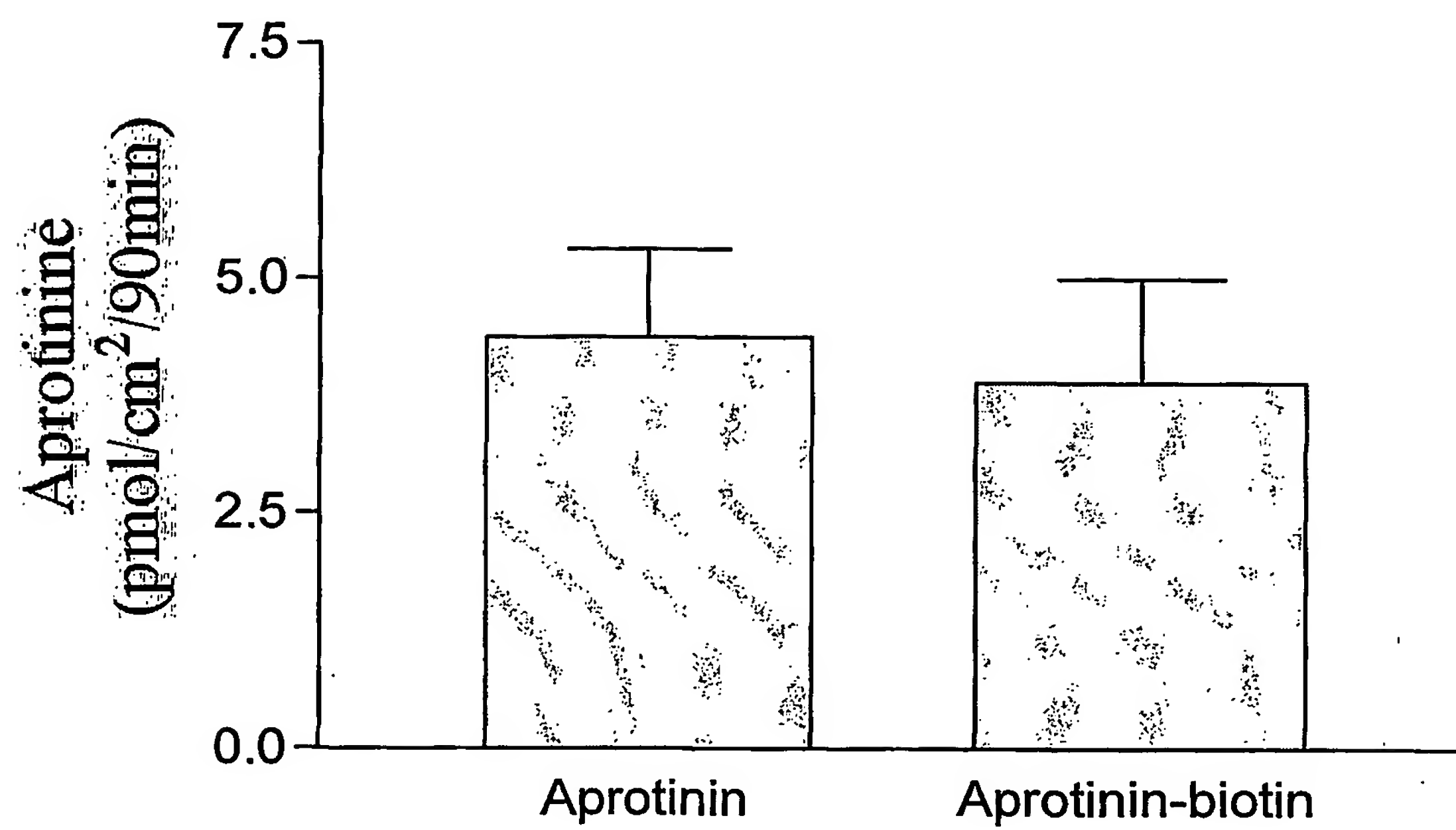


FIG. 10

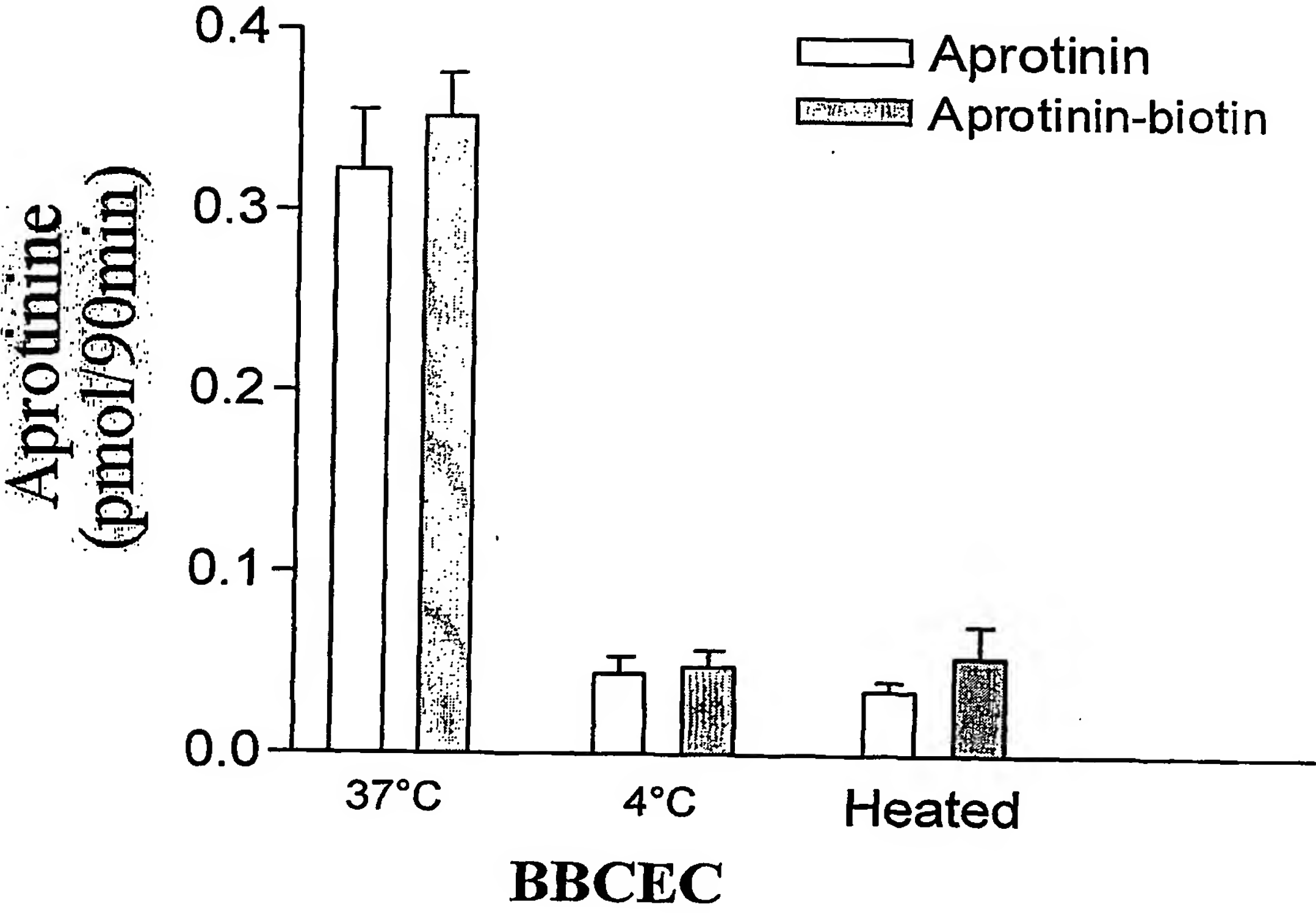


FIG. 11

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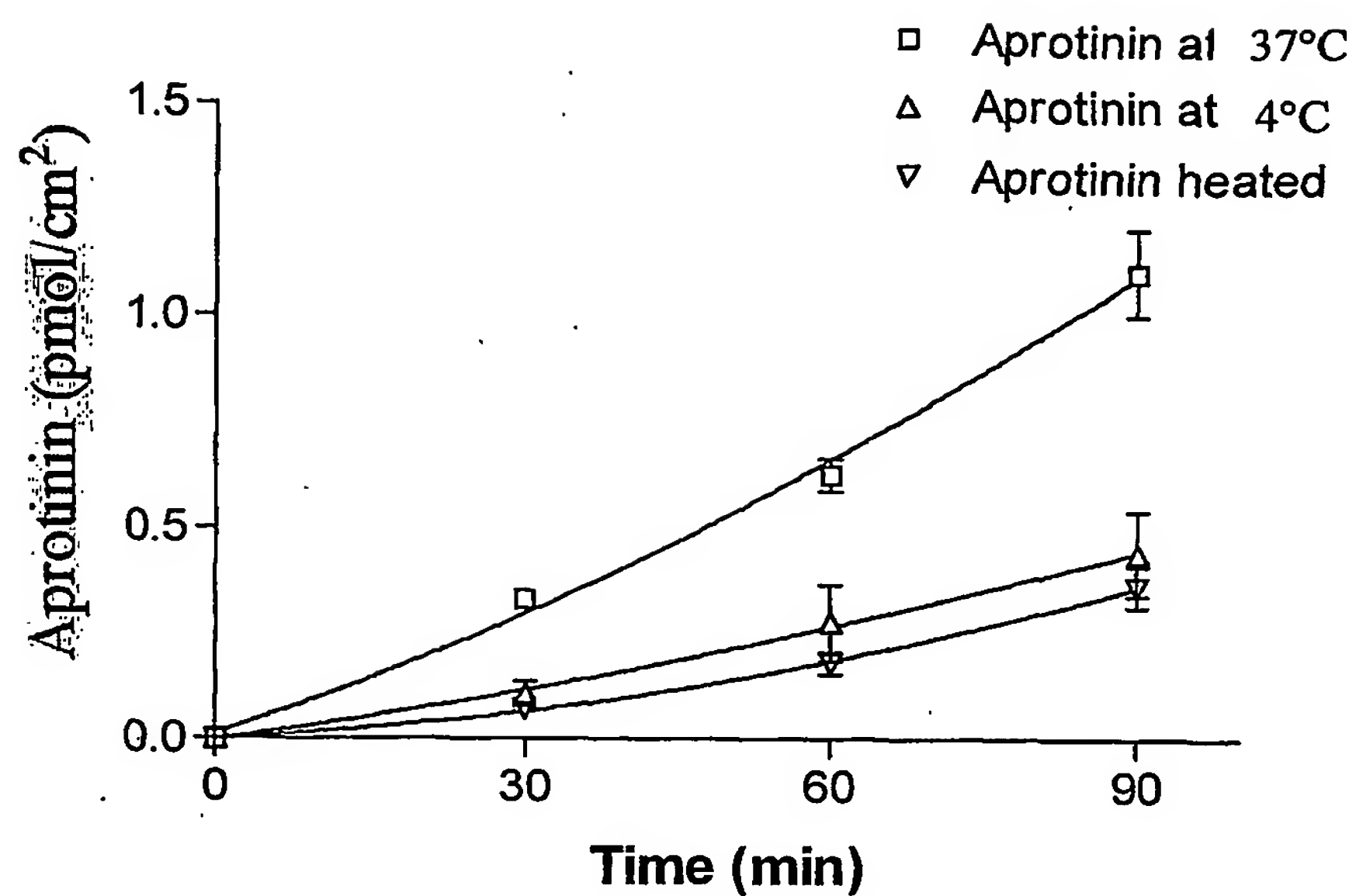


Fig. 12A

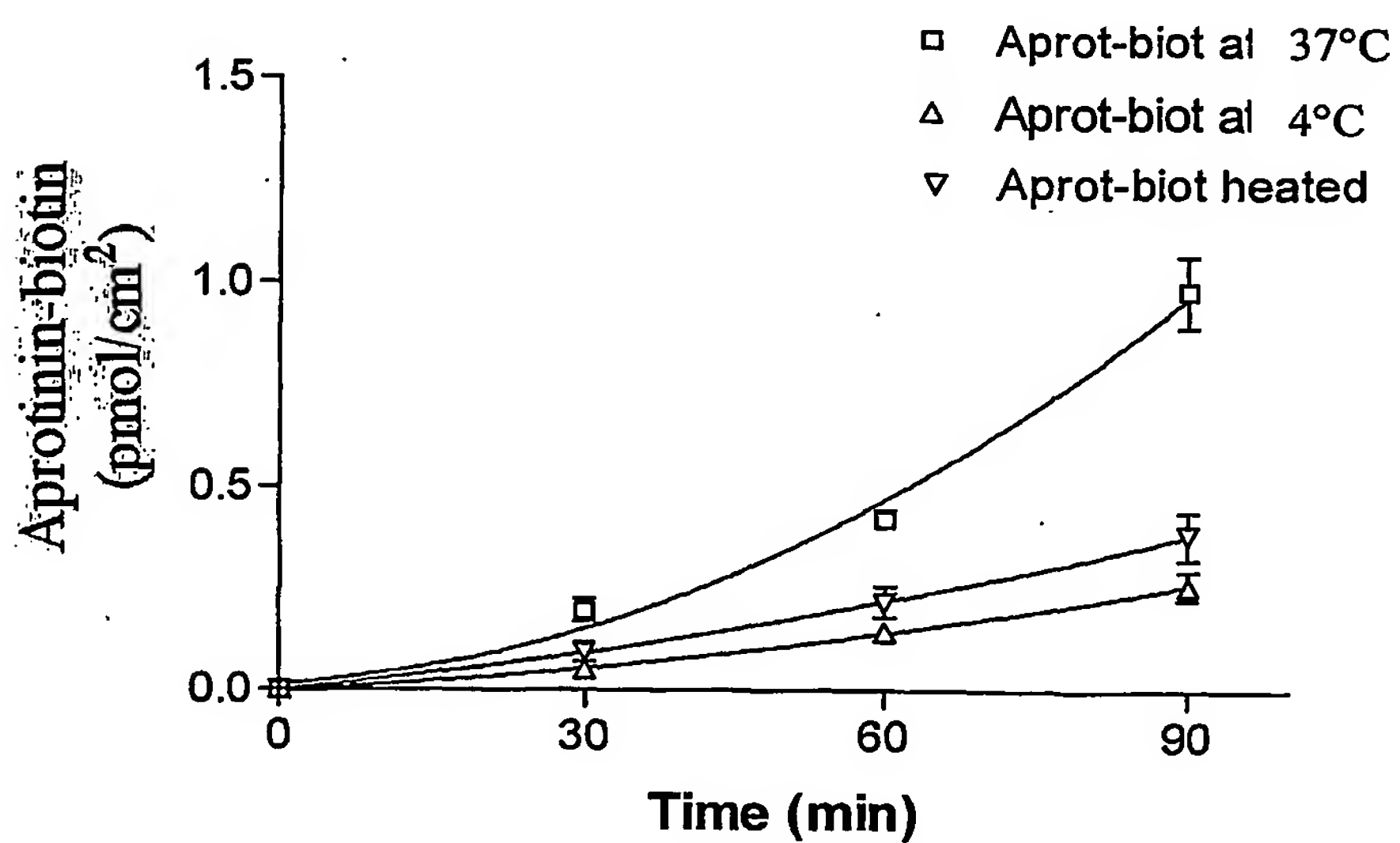


FIG. 12B

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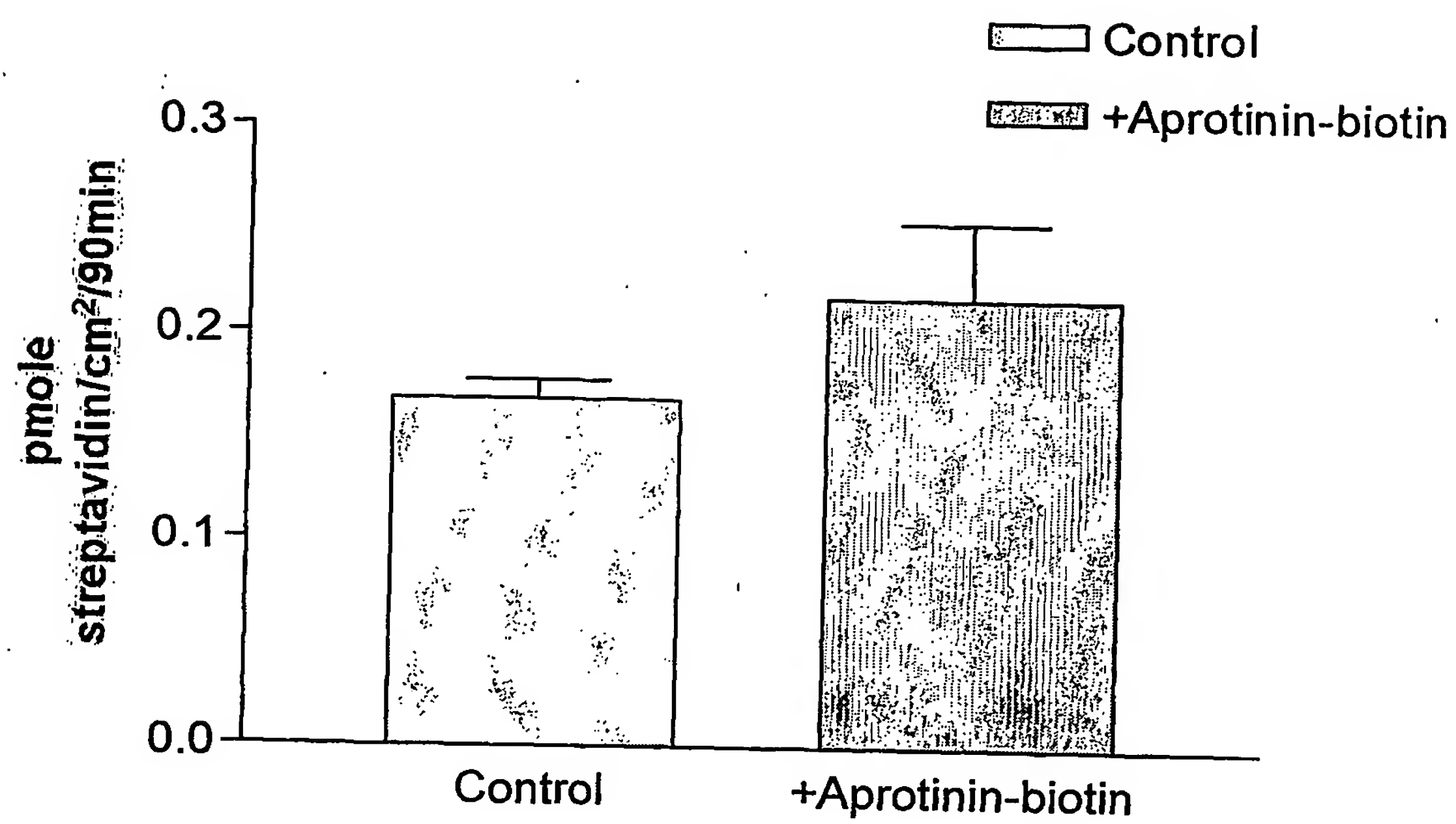


FIG. 13

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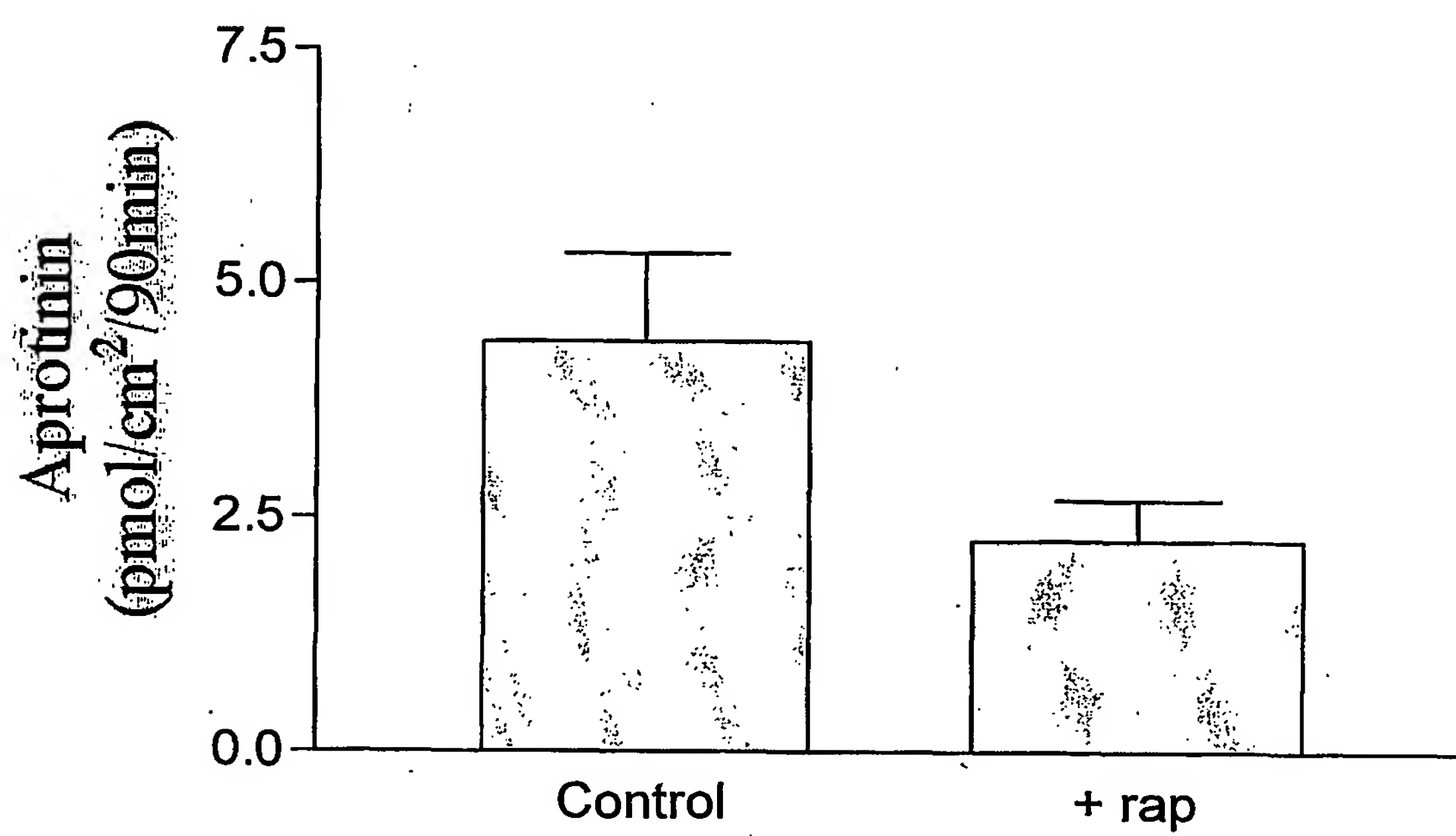
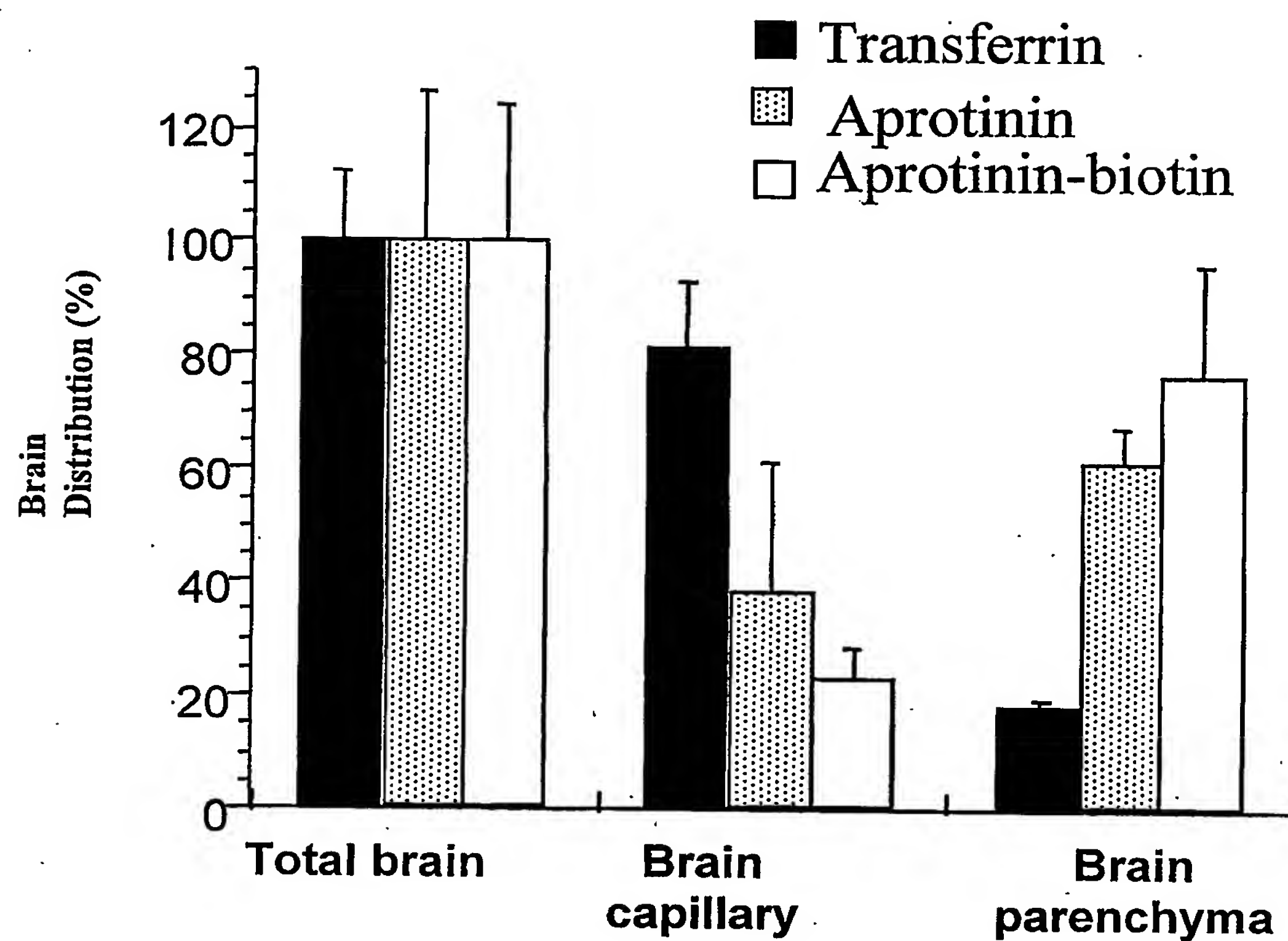


FIG. 14

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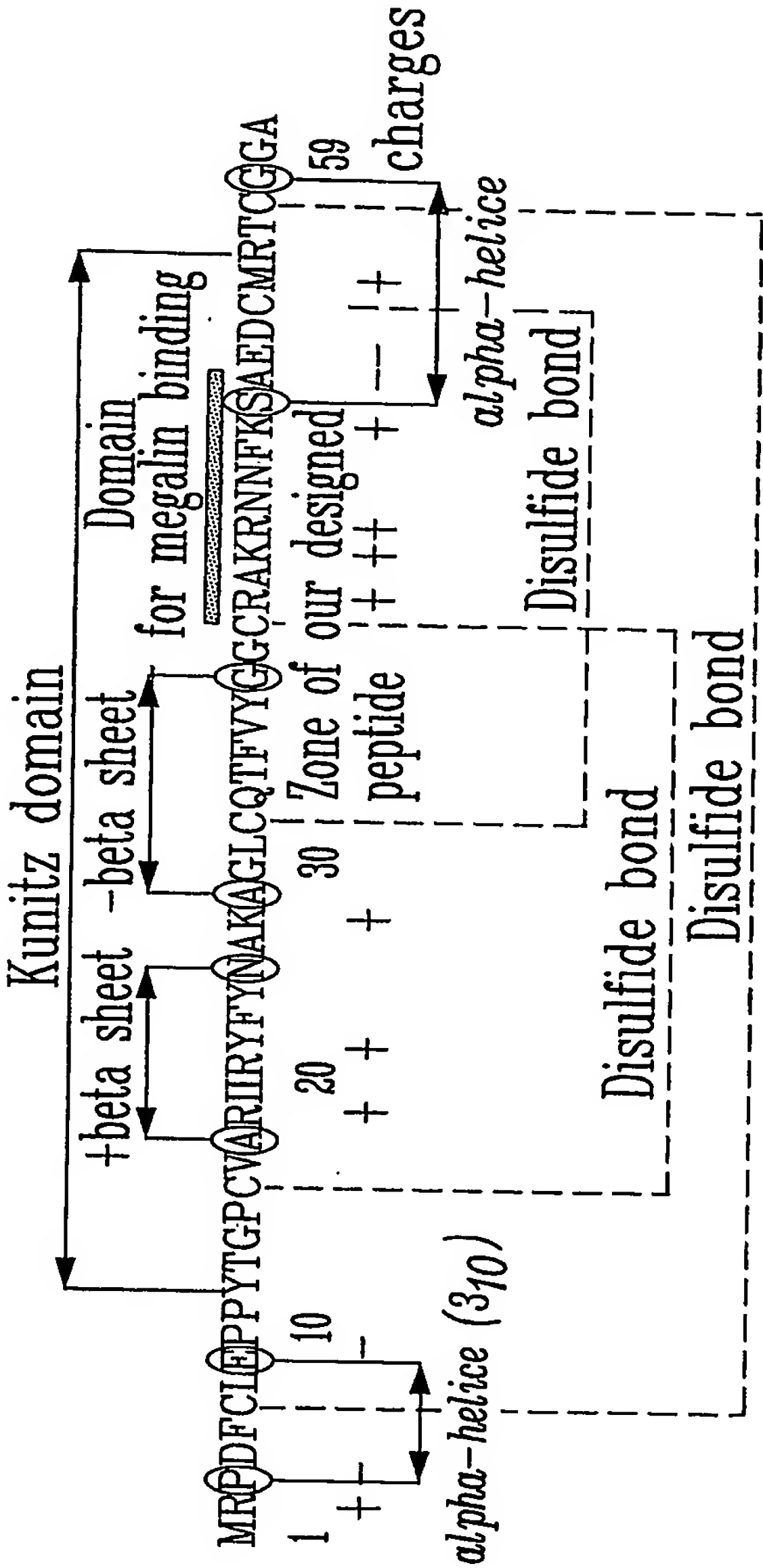


V_D for aprotinin in brain parenchyma = 3 μ l/100 g

FIG. 15

Synthetic-Aprotinin Sequence (net charge + 5)
Protein of 59 amino-acids, 6500 Da:

FIG. 16




- * Zone of our designed peptides
- * 4 nucleophiles amines=4 potential sites of conjugaison (residue 1,27,42,47)
- * 6 cysteines engaged in disulfides bonds
- * 2 alpha-helices and 2 beta sheets


Alignment between aprotinin
and three human proteins with a similar domain

FIG. 17

*Aprotinin-synthetic
bikunin HI-30
Amyloid beta A4 prot precursor
Kunitz-inhibitor 1 precursor*

									
310									
E	P	P	Y	T	G	P	C	K	A
L	G	Y	S	A	G	P	C	M	G
E	Q	A	E	T	G	P	C	R	A
A	S	N	K	V	G	R	C	R	G
GPC.. R..Y .T .C .F YG									
320									
A	K	A	G	L	C	Q	T	F	V
N	G	T	S	M	A	C	E	T	Q
F	Y	F	Y	N	D	V	T	E	G
R	Y	F	Y	N	D	V	T	E	G
R	W	Y	F	N	D	V	T	E	G
R	W	Y	F	N	D	V	T	E	G
330									

*Aprotinin-synthetic
bikunin HI-30
Amyloid beta A4 prot precursor
Kunitz-inhibitor 1 precursor*

									
350									
G	C	R	A	K	R	N	N	F	K
G	C	M	G	N	G	N	N	F	V
G	C	G	G	N	R	N	N	F	D
G	C	L	G	N	K	N	N	Y	L
GC GN.NNF .EE.C									
360									
S	A	E	D	C	M	R	T	C	G
T	E	K	E	C	L	Q	T	C	R
T	E	E	Y	C	M	A	V	C	G
R	E	E	E	C	I	L	A	C	R
370									
A	C	N	A	A	C	N	S	Q	A
S	L	L	K	T	S	-	-	M	E
380									
Kunitz domain									
390									

Minimal sequence of aprotinin for its interaction
with megalin

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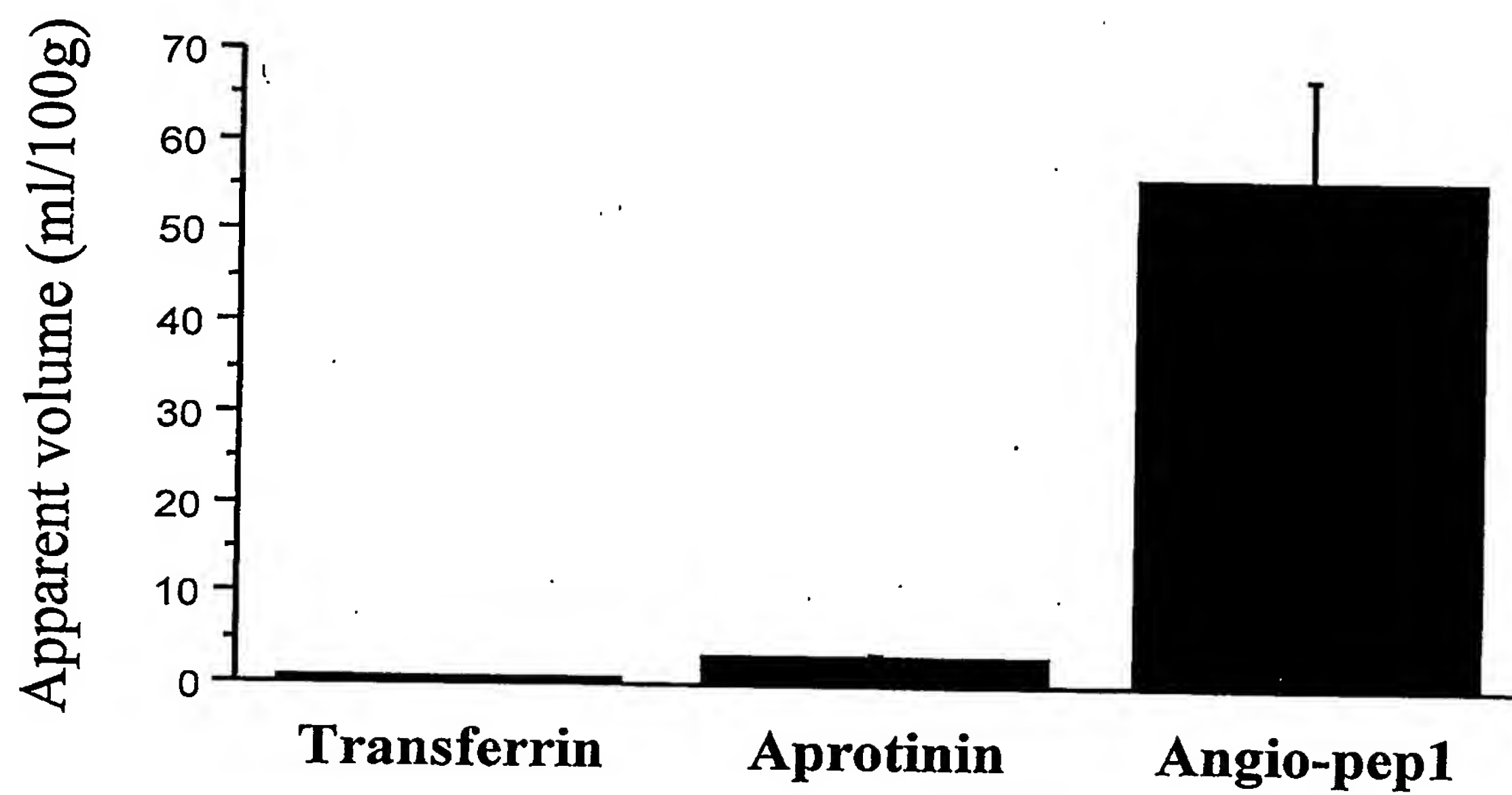
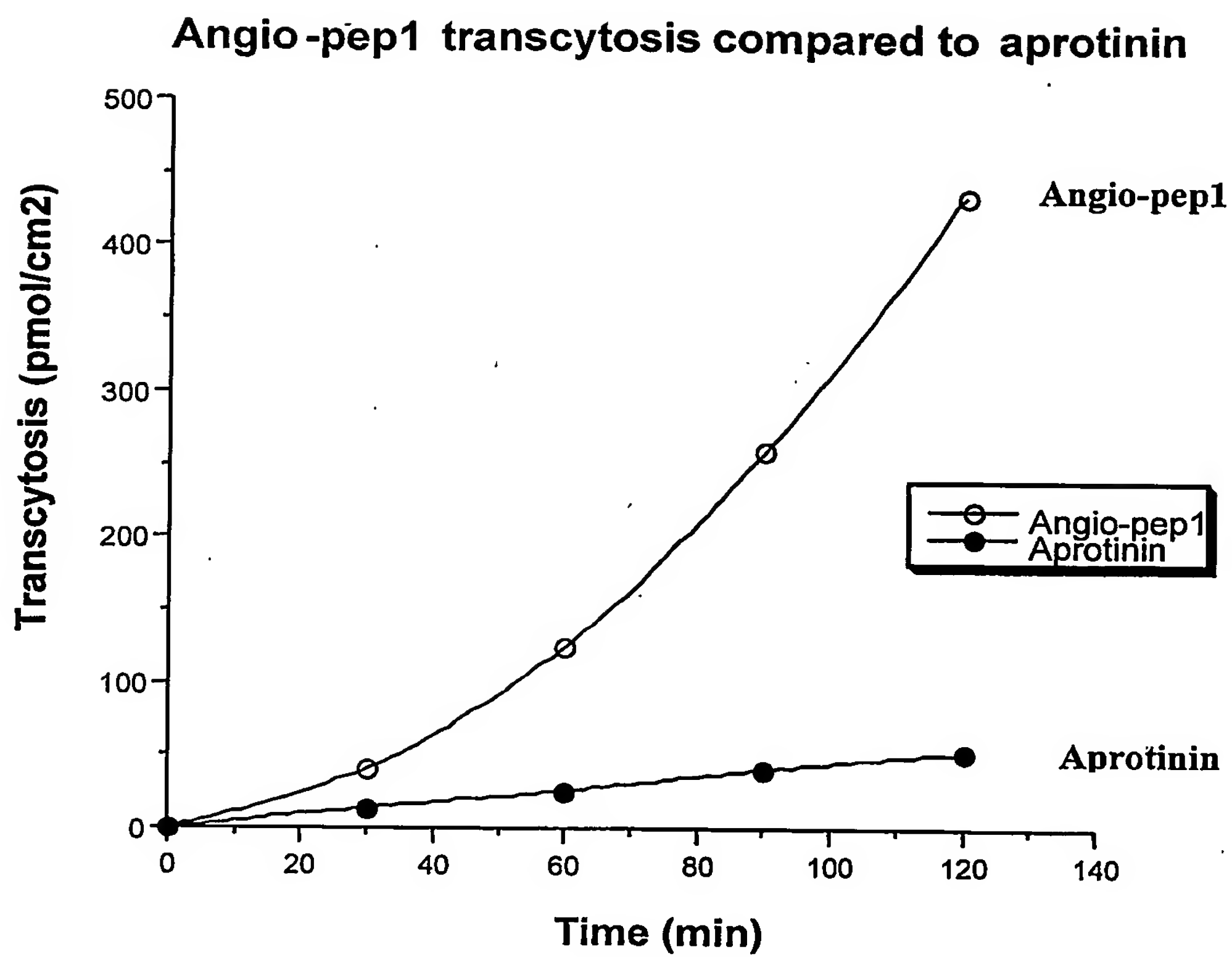


FIG. 18

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**FIG. 19**

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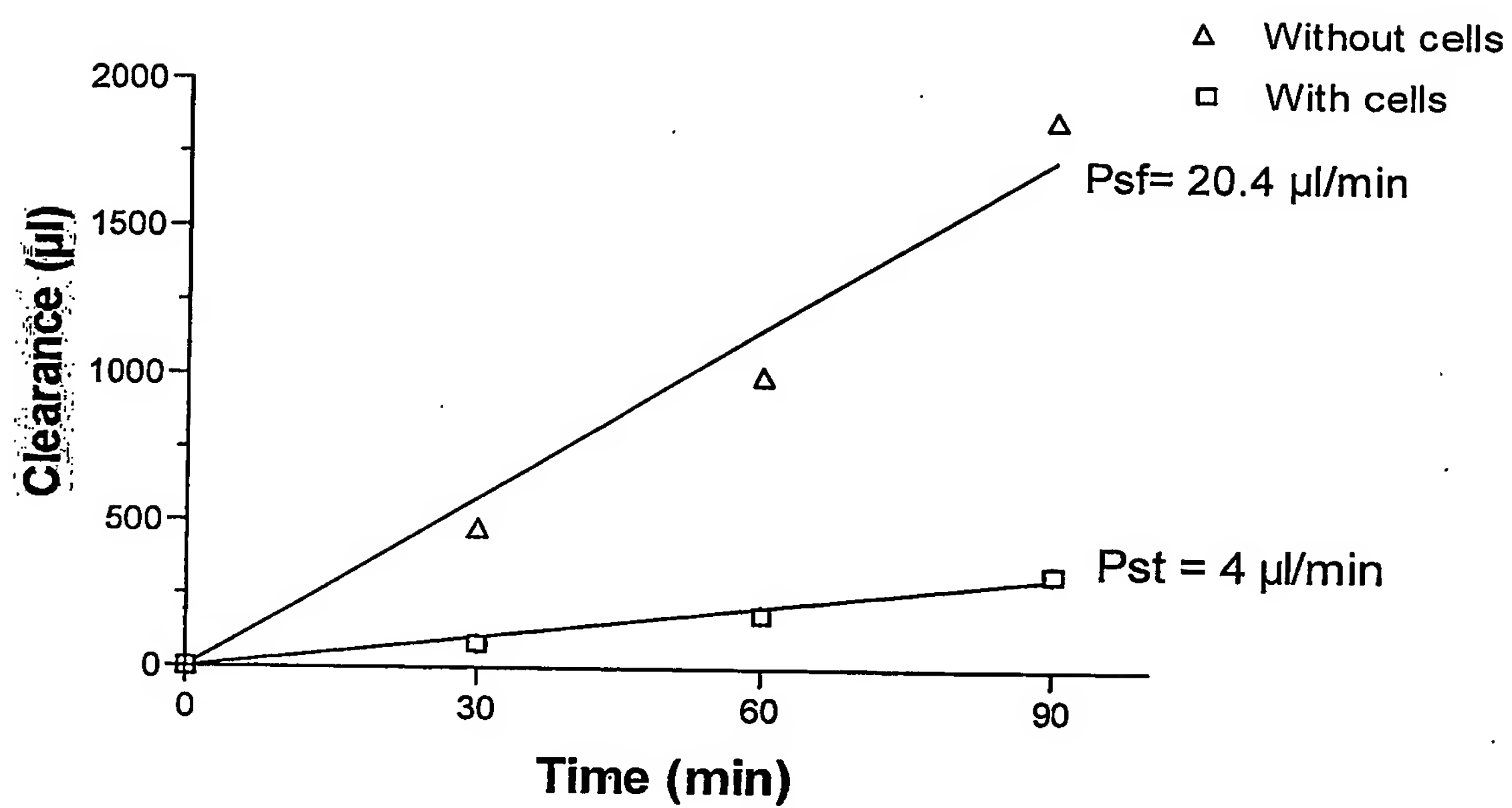


FIG. 20